Numb Expression and Asymmetric Versus Symmetric Cell Division in Distal Embryonic Lung Epithelium.

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Public Summary:
Proper balance between self-renewal and differentiation of lung specific progenitors is absolutely required for normal lung morphogenesis/regeneration. Therefore, understanding the behavior of lung epithelial stem/progenitor cells could identify innovative solutions for restoring normal lung morphogenesis and/or regeneration. The Notch inhibitor Numb is a key determinant of asymmetric or symmetric cell division, and hence cell fate. Yet Numb proximal-distal expression pattern and symmetric versus asymmetric division are uncharacterized during lung epithelial development. Herein, we find that the cell fate determinant Numb is highly expressed and asymmetrically distributed at the apical side of distal epithelial progenitors and segregated to one daughter cell in most mitotic cells. Knocking-down Numb in MLE15 epithelial cells significantly increased the number of cells expressing the progenitor cell markers Sox9/Id2. Furthermore, cadherin hole analysis revealed that most distal epithelial stem/progenitor cells in embryonic lungs divide asymmetrically; with their cleavage planes are predicted to bypass the cadherin hole, resulting in asymmetric distribution of the cadherin hole to the daughter cells. These novel findings provide evidence for asymmetric cell division in distal epithelial stem/progenitor cells of embryonic lungs, and provide a framework for future translationally oriented studies in this area.

Scientific Abstract: